

## **REMARKS**

The Applicants acknowledge the Examiner's comprehensive Office Action with appreciation. The Office acknowledges the Request for Continued Examination (RCE) filed on January 14, 2008. Claims 31-56, 59, and 61-63 remain pending in the application. The Office raises rejections under 35 USC § 102 and 35 USC § 103. The Office also indicates that Claims 55, 56, 59, and 62 are allowable.

The Office notes that Claim 63 was added by an Examiner's Amendment of October 11, 2006. The Applicants note that Claim 63 was inadvertently omitted from the Listing of Claims supplied with the RCE of January 14, 2008. Thus, Claim 63 is included in the present Listing of Claims with the identifier "previously presented." Moreover, with the instant Amendment, Claim 55 has been amended to correct a typographical error.

Claims 31-33, 36, 39, 41, 44, 54, and 63 are rejected under 35 USC § 102(b) as being anticipated by Iijima, et al. (*J. Med. Chem.*, **1978**, 21, 1320-1322). It is the position of the Office that compounds **1** (1-bromosinomeninone) and **3** (1-bromoisosinomenine) of Iijima, et al. anticipate the instantly claimed compounds when R<sub>1</sub> represents methyl, R<sub>2</sub> represents hydrogen, and both R<sub>3</sub> and R<sub>4</sub> and R<sub>5</sub> and R<sub>6</sub> together form oxo or R<sub>3</sub> and R<sub>4</sub> form an oxo group while R<sub>6</sub> represents alkoxy.

The Applicants respectfully submit that in the Listing of Claims filed with the Request for Continued Examination (RCE), Claim 31 recites the limitation "R<sub>3</sub> and R<sub>4</sub> together form oxo when X is fluorine, chlorine or iodine, or =N-OR<sub>8</sub> (wherein R<sub>8</sub> represents hydrogen or alkyl)." Therefore, compounds **1** and **3** of Iijima, et al. are not encompassed by the instant claim scope. Reconsideration and withdrawal of the rejection under 35 USC § 102(b) is respectfully requested.

Claims 31-33, 36, 38, 40, 41, 44, 52, 54, and 63 are further rejected under 35 USC § 103(a) for obviousness in view of the Iijima, et al. reference. It is the position of the Office that this reference discloses the synthesis and antinociceptive activity of 7-methoxycodine and that compounds **1** (1-bromosinomeninone), **2** (1-bromosinomenine), and **3** (1-bromoisosinomenine) disclosed in the reference meet

all the limitations of the instant claims when R<sup>1</sup> represents methyl and R<sup>2</sup> represents H, except that the variable X represents bromine instead fluorine, chlorine or iodine. The Office goes on the state that since bromine, chlorine, fluorine, and iodine all belong to the same halogen class, it would have been obvious to one skilled in the art to replace bromine with a different halogen to arrive at the instant compounds with the expectation that such compounds would also have antinociceptive activity.

The Applicants respectfully submit that the disclosure of the synthesis and antinociceptive activity of 7-methoxy codeine disclosed in the Iijima, et al. does not render obvious the instant compounds or their associated memory-improving activity, which activity is distinct from the antinociceptive activity disclosed in the reference. Moreover, the Applicants further submit that one skilled in the art would recognize that morphanane-type alkaloids are divided into two classes according to their absolute configuration: morphine/codeine alkaloids having a 9R, 13S, 14R configuration and sinomenine alkaloids. The morphine codeine alkaloids have been shown to possess strong anesthetic and analgesic action, and the sinomenine alkaloids have been shown to possess immunosuppressive, analgesic, antirheumatic, and anti-inflammatory activities (See attached References 1 and 2, which references are also listed on the enclosed Form PTO-1449). Thus, the Applicants respectfully submit that one skilled in the art would not have predicted the memory-improving activity associated with the instant compounds based on the disclosure of the Iijima, et al. reference. Reconsideration and withdrawal of the obviousness rejection is respectfully requested.

\* \* \* \* \*

Accordingly, entry of present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.


It should be apparent that the undersigned agent has made an earnest effort to place this application into condition for immediate allowance. If she can be of assistance to the Examiner in the elimination of any possibly-outstanding

insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call her at her below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,

THE FIRM OF HUESCHEN AND SAGE

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Enclosure: Form PTO-1449 and Accompanying References; Listing of Claims and  
Postal Card Receipt

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**THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER  
OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION,  
DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO  
DEPOSIT ACCOUNT NO. 08,3220.**